figwort mosaic virus 34S promoter, a DNA sequence of interest heterologous to said promoter and a transcript termination region functional in a plant cell.

REMARKS

Pending Claims

Claims 20, 22-28, 30, 33-36 and 43 are pending in the present application.

Status of the Application

The finality of the previous Office Action is withdrawn in the latest Office Action, for the reason of a new ground of rejection made therein.

Amendments

The title of the application is amended to more clearly identify the subject matter of the claimed invention.

The amendment to Claim 20 is intended to clarify Applicants' invention. Support for this amendment is found throughout the specification, particularly in the examples and in the following descriptions: in the summary of the invention provided in page 4 of the specification, describing the constitutive nature of FMV 34S promoter; and at the middle of page 7, where the activity of the 34S promoter in transgenic plants is described.

The Invention

In the Office Action the Examiner suggests that Applicants are shifting to a changed definition of promoter, one which focuses on the TATA box and its sequence. Applicants are not sure in which of their remarks the Examiner suspects such a shift. In any case, Applicants submit that the claims, and not any remarks, have been and should remain the focus of any discussion of the invention.

The claims as presented in this amendment are well supported by the disclosure as originally filed. The amended identification of the promoter as one capable of constitutive activity focuses attention on Applicants' the 34S FMV promoter, which has the claimed characteristics in transgenic plants.

35 U.S.C. § 112, Second Paragraph Rejection

Applicants gratefully acknowledge the withdrawal of the rejections of Claim 20, 22-28, 30, 33-36 and 43 under this provision, in view of Applicants' amendment to the claims filed January 18, 1993.

35 U.S.C. § 112, First and Second Paragraph Rejection

Applicants gratefully acknowledge the withdrawal of the rejection of Claims 20, 22-28, 30, 33-36 and 43 under the above provisions, in view of Applicants' amendment to the claims filed January 18, 1993.

35 U.S.C. § 112, First Paragraph Rejection

Applicants gratefully acknowledge the withdrawal of the rejection of Claims 20, 22-28, 30, 33-36 and 43 under this provision, in view of Applicants' amendment to the claims filed January 18, 1993.

35 U.S.C. § 102(a) Rejection

The Examiner has reinstated the rejection of Claims 20, 22-27 and 33-35 under §102(a) in view of Gowda *et al.* or Wu *et al.* and Claims 20, 22-27 and 33-36 under §102(a) in view of Goldberg *et al.*, for the reason that the previously submitted §1.131 declaration used to overcome these references was not signed by each of the inventors.

Applicants submit herein a §1.131 declaration signed by all of the inventors and demonstrating completion of the invention prior to November 13, 1988.

This declaration removes the Gowda *et al.*, Wu *et al.* and Goldberg *et al.* references as prior art, and Applicants respectfully request the withdrawal of the §102(a) rejection.

35 U.S.C. § 103

Claims 20, 22-28, 30, 33-36 and 43 are rejected under 35 U.S.C. § 103 over Shah *et al.* and Sanders *et al.* taken with Richins *et al.*, or Gowda *et al.*, or Wu *et al.* or Goldberg *et al.* This rejection is respectfully traversed as follows.

Shah *et al.* describes DNA constructs for expression using Cauliflower Mosaic Virus (CaMV) 35S promoters. The other primary reference, Sanders *et al.*, compares the strength of CaMV 35S and nopaline synthase (nos) promoters in leaves from transgenic plants, teaching that higher levels of expression are possible using the 35S promoter.

The Examiner states that these primary references disclose all features of Applicants' invention except for specifying the FMV 34S promoter as an alternative viral promoter to the 35S promoter of CaMV.

Applicants do not dispute the characterization of Shah *et al.* as teaching the use of the 35S promoter of CaMV in producing transgenic plants. Applicants submit, however, that the 34S promoter of FMV was not known to be a constitutive promoter under even the most generous reading of the cited references. The declaration of Dr. Sanger previously submitted in this case rebuts any presumption that the 34S promoter of FMV was obvious or known to be an equivalent constitutive promoter to the CaMV 35S promoter at the time of the invention.

The examiner has failed to provide a citation or point to language in any reference which taught or suggested that the FMV genome was an "alternative" to the CaMV 35S promoter at the effective filing date of this application. In fact, no reference characterizes any promoter of FMV as having any known characteristics, whatsoever. Clearly, there is no teaching or suggestion in the primary references that a

constitutive promoter is expected in FMV, and as to the Gowda *et al.*, Wu *et al.* and Goldberg *et al.* secondary references, as previously discussed with regard to the §102(a) rejection, Applicants submit herewith a declaration which removes these secondary references as prior art.

The Examiner characterizes the secondary references, presumably including the remaining Richins *et al.* secondary reference, as disclosing an "FMV 34S promoter which was analogous in structure and strong expression characteristics with the well-known CaMV 35S promoter long used in recombinant constructs in transgenic plants". In a subsequent §103 rejection Richins *et al.* is described as teaching that the FMV promoter sequence is analogous to the CaMV 35S promoter in position, structure and function. Thus, the Examiner finds that it would have been obvious to express genes from FMV as "yet another strong viral promoter" with a reasonable expectation of success. The Examiner submits that these primary and secondary references, along with the general knowledge in the art regarding plant gene promoters and promoters of other viruses, provides a reasonable expectation of success for using an "analogous" promoter from 34S FMV.

The fact is, however, that the record does not support the contention that the 34S FMV promoter was known to one ordinarily skilled in the art, let alone expected to be a constitutive promoter analogous to or an alternative for the 35S promoter of CaMV. The similarities noted by Richins *et*

al. between the genomic sequence of CaMV allowed the identification of suspected promoter TATA regions. The identification of a potential promoter site does not determine that a particular region will provide a promoter, and, particularly one which would function as a constitutive promoter.

The Examiner states that CaMV 35S was not the only plant viral promoter known and used at the time of the invention. An alternative reference for any other known plant viral promoter is not provided, let alone a reference describing one which was well understood and characterized. Based on the alleged knowledge of regulatory sequences of "any given gene", one ordinarily skilled in the art is viewed for the examples as capable of drawing conclusions about the strength and function of the regulatory elements of possible FMV promoters.

To render an invention obvious, the prior art must not only suggest the invention and suggest that it is reasonably likely to succeed, but further "both the suggestion and the expectation of success must be founded in the prior art, not in the applicants disclosure." *In re Dow Chemical*, 837 F.2d 469, 472 (Fed. Cir. 1988).

In the instant case, based on the prior art, one could have suspected that FMV had one or more promoter binding regions. Richins *et al.* provides the sequence of FMV, which, like CaMV, is a caulimovirus, and it might even have even been obvious to try sequences from among the sequence

disclosed by Richins *et al.* in an effort to determine if a promoter was present, or to learn the potential usefulness of such a promoter.

Dr. Sanger points out the difficulty in having expectations or making conclusions on sequence comparisons alone, even among related caulimoviruses (pages 3-4 of Sanger declaration). Dr. Sanger declares that the state of the art, even now, five years after the invention, does not allow general conclusions about a promoter function or the expected strength of the activity based on sequence comparisons (pages 3-4 of Sanger declaration). Even based on the related CaMV genome, then, there was as much reason to doubt the existence of such a promoter in FMV, as to expect it. Until at least one other promoter was characterized and shown to be analogous to the well known 35S promoter of CaMV, no one could be sure if any other promoter existed which was like the 35S promoter of CaMV. The equally plausible alternative was that the 35S promoter of CaMV was unique among viral promoters in function and activity.

Without having tested for promoter activity, the authors of Richins *et al.* can only speculate as to the location of any potential FMV promoter. Richins *et al.* clearly states that the suggested location of a FMV promoter based on TATA sequences within the large intergenic area was a <u>subjective</u> choice, as other TATA-like sequences are observed in this region (page 8464, second paragraph). Richins *et al.* further focuses on the intergenic region <u>downstream</u> of the FMV

promoter of the instant Application (Figure 5, page 8460). The ORF of gene VI is noted as being the least conserved region among the sequences of those caulimoviruses which were examined (bottom of 8458). The 5' upstream region which Applicants determined to be so important to the strength and activity of the 34S FMV promoter lies precisely within this poorly conserved region.

The Examiner has not pointed out those teachings about other genes, promoters or viruses which could be combined with the teachings in Richins *et al.* to suggest to one of ordinary skill in the art that the 34S promoter would be expected to demonstrate a certain level of activity or a particular constitutive function in a plant cell, or would be expected to be comparable in any way, for that matter, with the 35S promoter of CaMV. Applicants' disclosure teaches this for FMV, it does not come from any suggestion in the prior art, and the prior art does not provide an expectation of success for Applicants' claimed invention.

In view of the above, Applicants submit that the rejection under 35 U.S.C. §103 over the combination of Shah *et al.* and Sanders *et al.* taken with Richins *et al.* or Gowda *et al.* or Wu *et al.* or Goldberg *et al.* be withdrawn.

35 U.S.C. § 103

Claims 20, 22-28, 30, 33-36 and 43 are rejected under 35 U.S.C. § 103 over Shah *et al.* and Sanders *et al.* taken with

Richins *et al.*and Shepherd *et al.* This rejection is respectfully traversed as follows.

Shah *et al.*, Sanders *et al.* and Richins *et al.* are discussed more fully above. These references do not provide one with the instantly claimed invention.

Shepherd *et al.* is cited by the Patent Office as demonstrating a broad host range for FMV and high titer obtainable with FMV in plant host cells. The Examiner further states, however, that concern expressed by Applicants' regarding titer is misplaced. Applicants are not sure what aspect of this concern the Examiner considers misplaced, as Applicants' comments regarding titer were a response to the position of the Examiner that the high titer shown for FMV in Shepherd *et al.* made it reasonable to expect the promoter to be one which is highly expressed. (See page 9 of March 19, 1992 Office Action).

If the Examiner is stating a position that a high titer does not provide evidence of promoter strength, Applicants agree. If the Examiner is maintaining that the high titer reported for the adapted DxS strain of FMV in Shepherd *et al.* would have lead one to expect a promoter in FMV showing strong expression characteristics or constitutive expression in transgenic plants, then Applicants disagree, and maintain their concern about the Examiners' position on titer.

Applicants agree that Shepherd *et al.* teaches that FMV is amenable to cloning manipulation, as Shepherd *et al.* provides a restriction map for the virus.

As to the cited teachings regarding the promoter itself, the Examiner states that Shepherd *et al.* echoes the disclosure in Richins *et al.* that the 34S promoter of FMV was analogous to CaMV 35S in position, structure, function and was expected to have strong expression characteristics. The Examiner further states that Shepherd *et al.* compared CaMV and FMV promoters.

In light of the fact that Shepherd *et al.* does not disclose an FMV sequence, and reports no tests of FMV promoter activity, Applicants submit that a comparison of promoters is simply not present in Shepherd *et al.* In fact, Shepherd *et al.* never discusses the region of Applicants' 34S promoter at all, other than to indicate a suspected correlation to the gene VI region of CaMV, with intergenic regions to both sides. However, the genome is noted as being particularly non-homologous in the gene VI region (page 1672, second column).

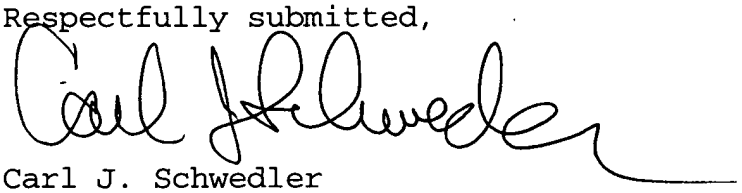
In short, Shepherd *et al.* presents no analysis and no data which would suggest to one ordinarily skilled in the art that FMV is expected to have a promoter similar in expression characteristics to the 35S promoter of CaMV.

In view of the above, Applicants submit that the rejection under 35 U.S.C. 103 over the combination of Shah *et al.* and Sanders *et al.* taken with Richins *et al.* and Shepherd *et al.* be withdrawn.

CONCLUSION

In view of the above, Applicants submit that the instant application is in immediate condition for allowance and early notice to this effect is solicited. If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the application, the Examiner is invited to contact the undersigned at (916)753-6313.

Respectfully submitted,



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Enclosure: Declaration of Drs. Comai, Sanger and Daubert